

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Serial No. : 09/836,705  
Applicants : Yuki ABE et al.  
Filed : April 17, 2001  
For : METHODS FOR PRODUCING ML-236B,  
A PRAVASTATIN PRECURSOR,  
USING A HOST CELL TRANSFORMED  
WITH *mlcR*, A TRANSCRIPTION  
FACTOR



Art Unit : 1652  
Examiner : Kathleen M. Kerr  
Docket No. : 01149/HG  
Customer No. : 01933  
Confirmation No. : 7090

DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

ATTENTION: MAIL STOP AMENDMENT

S I R :

The undersigned declares as follows:

1. I am a coinventor of the above-identified patent application.

2. I graduated from the University of Tokyo  
in the year 1994, and I received the degree of  
Ph.D.

3. I have worked for Sankyo Company, Limited of Tokyo,  
Japan, since the year 1996, and I presently hold the position  
of a Scientist.

4. With regard to Yu et al., Applied and Environmental Microbiology, (1995), 61(6), 2372-2377, which was applied in a prior art rejection in the July 15, 2004 Office Action, I carried out an analysis of the homology between *Aspergillus parasiticus* aflR and *Aspergillus flavus* AflR, and *Penicillium citrinum* mlcR (as in the present invention) using DNASIS software. The results of such analysis are set forth in the following Tables 1 and 2.

Table 1 cDNA sequence homology between *mlcR* and *aflR*.

cDNA sequence	Homology(%)		
	<i>mlcR</i>	<i>A. parasiticus aflR</i>	<i>A. flavus aflR</i>
<i>Penicillium citrinum mlcR</i>	100	no homology	no homology
<i>Aspergillus parasiticus aflR</i>	no homology	100	96.9
<i>Aspergillus flavus aflR</i>	no homology	96.9	100

Table 2 Amino acid sequence homology between *MlcR* and *AflR*.

Amino Acid sequence	Homology(%)		
	<i>MlcR</i>	<i>A. parasiticus AflR</i>	<i>A. flavus AflR</i>
<i>Penicillium citrinum MlcR</i>	100	no homology	no homology
<i>Aspergillus parasiticus AFLR</i>	no homology	100	94.2
<i>Aspergillus flavus AFLR</i>	no homology	94.2	100

The above results show that the cDNA (nucleotide) homology between the two *aflR* genes is 96.9%, and the amino acid homology between the two *aflR* genes is 94.2%. The above results also demonstrate that the *mlcR* gene reveals no homology with both *aflR* genes.

5. Regarding WO 01/12814 which was applied with Yu et al. in a prior art rejection in the July 15, 2004 Office Action, in the specification of WO 01/12824, it was shown that a gene cluster containing six hypothetical genes could enhance the production of ML-236B. But it was not shown which gene or which combination of genes could really work and enhance said production.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: Oct 6 , 2004

By:

Yuki Abe

Name:

阿部 有生